=> d ibib abs ind l8 1-9

L8 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:285012 HCAPLUS
DOCUMENT NUMBER: 141:138762
TITLE: CTLA-4 blockade in combination with **xenogeneic** DNA vaccines enhances T-cell responses, tumor immunity and autoimmunity to self antigens in animal and cellular model systems
AUTHOR(S): Gregor, Polly D.; **Wolchok, Jedd D.**; Ferrone, Cristina R.; Buchinshky, Heidi; Guevara-Patino, Jose A.; Perales, Miguel-Angel; Mortazavi, Fariborz; Bacich, Dean; Heston, Warren; Latouche, Jean-Baptiste; Sadelain, Michel; Allison, James P.; Scher, Howard I.; **Houghton, Alan N.**
CORPORATE SOURCE: Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Vaccine (2004), 22(13-14), 1700-1708
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Xenogeneic** DNA vaccination can elicit tumor immunity through T cell and antibody-dependent effector mechanisms. Blockade of CTLA-4 engagement with B7 expressed on APCs has been shown to enhance T cell-dependent immunity. We investigated whether CTLA-4 blockade could increase T-cell responses and tumor immunity elicited by DNA vaccines. CTLA-4 blockade enhanced B16 tumor rejection in mice immunized against the **melanoma** differentiation antigens tyrosinase-related protein 2 and gp100, and this effect was stronger when anti-CTLA-4 was administered with booster vaccinations. CTLA-4 blockade also increased the T-cell responses to prostate-specific membrane antigen (PSMA) when given with the second or third vaccination. Based on these pre-clin. studies, we suggest that anti-CTLA-4 should be tested with **xenogeneic** DNA vaccines against cancer and that special attention should be given to sequence and schedule of administration.
CC 15-2 (Immunochemistry)
ST cancer vaccine CTLA4 antibody cytotoxic T lymphocyte
IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRP-2 (tyrosinase-related protein 2); anti-CTLA-4 enhances T-cell responses and tumor immunity elicited by DNA cancer vaccines)
IT Immunostimulants
(adjuvants; anti-CTLA-4 enhances T-cell responses and tumor immunity elicited by DNA cancer vaccines)
IT **Melanoma**
Plasmid vectors
(anti-CTLA-4 enhances T-cell responses and tumor immunity elicited by DNA cancer vaccines)
IT CTLA-4 (antigen)
DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-CTLA-4 enhances T-cell responses and tumor immunity elicited by DNA cancer vaccines)
IT Intestine, neoplasm
(colon, adenocarcinoma; anti-CTLA-4 enhances T-cell responses and tumor immunity elicited by DNA cancer vaccines)
IT T cell (lymphocyte)
(cytotoxic; anti-CTLA-4 enhances T-cell responses and tumor immunity

elicited by DNA cancer vaccines)
IT Glycoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gp100; anti-CTLA-4 enhances T-cell responses and tumor immunity elicited by DNA cancer vaccines)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, to CTLA-4; anti-CTLA-4 enhances T-cell responses and tumor immunity elicited by DNA cancer vaccines)
IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor-associated, PSMA (prostate-specific membrane antigen); anti-CTLA-4 enhances T-cell responses and tumor immunity elicited by DNA cancer vaccines)
IT Vaccines
(tumor; anti-CTLA-4 enhances T-cell responses and tumor immunity elicited by DNA cancer vaccines)
IT Antitumor agents
(vaccines; anti-CTLA-4 enhances T-cell responses and tumor immunity elicited by DNA cancer vaccines)
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:192946 HCAPLUS
DOCUMENT NUMBER: 140:355335
TITLE: Immunity to cancer through immune recognition of altered self: studies with **melanoma**
AUTHOR(S): Guevara-Patino, Jose A.; Turk, Mary Jo; **Wolchok, Jedd D.**; **Houghton, Alan N.**
CORPORATE SOURCE: Memorial Sloan-Kettering Cancer Center and the Weill Graduate School of Medical Sciences, Medical School of Cornell University, New York, NY, 10021, USA
SOURCE: Advances in Cancer Research (2003), 90, 157-177, 1 plate
CODEN: ACRSAJ; ISSN: 0065-230X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The adaptive immune system is capable of recognizing cancer through T and B-cell receptors. However, priming adaptive immunity against self antigens is potentially a difficult task. Presentation of altered self to the immune system is a strategy to elicit immunity against poorly immunogenic antigens. We have shown that immunization with conserved paralogues of tumor antigens can induce adaptive immunity against self antigens expressed by cancer. Remarkably, cancer immunity elicited by closely related paralogues can generate distinct adaptive immune responses, either antibody or T-cell dependent. Cancer immunity induced by **xenogeneic** immunization follows multiple and alternative pathways. The effector phase of tumor immunity can be mediated by cytotoxic T cells or macrophages and perhaps natural killer cells for antibody-dependent immunity. Helper CD4+ T cells are typically, but not always, required to generate immunity. Autoimmunity is frequently observed following immunization. Cancer immunity and autoimmunity use overlapping mechanisms, and therefore they are difficult to uncouple, but distinct pathways can be discerned that open the eventual possibility of uncoupling tumor immunity from autoimmunity. Studies examining the mol.

basis for immunogenicity of conserved paralogues are facilitating the development of new strategies to rationally design vaccines that trigger adaptive immune responses to cancer.

CC 15-0 (Immunochemistry)
ST review B cell receptor autoimmunity autoantigen antibody
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(autoantigens; immunity to cancer through immune recognition of altered self)
IT Immunity
(autoimmunity; immunity to cancer through immune recognition of altered self)
IT T cell (lymphocyte)
(cytotoxic; immunity to cancer through immune recognition of altered self)
IT CD4-positive T cell
Neoplasm
(immunity to cancer through immune recognition of altered self)
IT Antibodies and Immunoglobulins
BCR (B cell receptors)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunity to cancer through immune recognition of altered self)
IT Lymphocyte
(natural killer cell; immunity to cancer through immune recognition of altered self)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:345937 HCAPLUS
DOCUMENT NUMBER: 139:34865
TITLE: A Single Heteroclitic Epitope Determines Cancer Immunity After **Xenogeneic** DNA Immunization Against a Tumor Differentiation Antigen
AUTHOR(S): Gold, Jason S.; Ferrone, Cristina R.; Guevara-Patino, Jose A.; Hawkins, William G.; Dyall, Ruben; Engelhorn, Manuel E.; **Wolchok, Jedd D.**; Lewis, Jonathan J.; **Houghton, Alan N.**
CORPORATE SOURCE: Memorial Sloan-Kettering Cancer Center, Cornell University, New York, NY, 10021, USA
SOURCE: Journal of Immunology (2003), 170(10), 5188-5194
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Successful active immunization against cancer requires induction of immunity against self or mutated self Ags. However, immunization against self Ags is difficult. **Xenogeneic** immunization with orthologous Ags induces cancer immunity. The present study evaluated the basis for immunity induced by active immunization against a **melanoma** differentiation Ag, gp100. Tumor rejection of **melanoma** was assessed after immunization with human gp100 (hgp100) DNA compared with mouse gp100 (mgp100). C57BL/6 mice immunized with **xenogeneic** full-length hgp100 DNA were protected against syngeneic **melanoma** challenge. In contrast, mice immunized with hgp100 DNA and given i.p. tolerizing doses of the hgp100 Db-restricted peptide, hgp10025-33, were incapable of rejecting tumors. Furthermore, mice immunized with DNA constructs of hgp100 in which the hgp10025-27 epitope was substituted with the weaker Db-binding epitope from mgp100 (mgp10025-27) or a mutated epitope unable to bind Db did not reject B16 **melanoma.** Mice

immunized with a minigene construct of hgp10025-33 rejected B16 **melanoma**, whereas mice immunized with the mgp10025-33 minigene did not develop protective tumor immunity. In this model of **xenogeneic** DNA immunization, the presence of an hgp100 heteroclitic epitope with a higher affinity for MHC created by three amino acid (25 to 27) substitutions at predicted minor anchor residues was necessary and sufficient to induce protective tumor immunity in H-2b mice with **melanoma.**

CC 15-2 (Immunochemistry)

ST **melanoma** epitope DNA immunization tumor differentiation antigen

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(differentiation, tumor; single heteroclitic epitope dets. cancer immunity after **xenogeneic** DNA immunization against a tumor differentiation antigen)

IT **Melanoma**
(inhibitors; single heteroclitic epitope dets. cancer immunity after **xenogeneic** DNA immunization against a tumor differentiation antigen)

IT Epitopes
Immunization
(single heteroclitic epitope dets. cancer immunity after **xenogeneic** DNA immunization against a tumor differentiation antigen)

IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(single heteroclitic epitope dets. cancer immunity after **xenogeneic** DNA immunization against a tumor differentiation antigen)

IT 212370-40-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(single heteroclitic epitope dets. cancer immunity after **xenogeneic** DNA immunization against a tumor differentiation antigen)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:273846 HCAPLUS

DOCUMENT NUMBER: 139:358123

TITLE: Long-Term Survival of Dogs with Advanced Malignant **Melanoma** after DNA Vaccination with **Xenogeneic** Human Tyrosinase: A Phase I Trial

AUTHOR(S): **Bergman, Philip J.**; McKnight, Joanne; Novosad, Andrew; Charney, Sarah; Farrelly, John; Craft, Diane; Wulderk, Michelle; Jeffers, Yusuf; Sadelain, Michel; Hohenhaus, Ann E.; Segal, Neil; Gregor, Polly; Engelhorn, Manuel; Riviere, Isabelle; **Houghton, Alan N.**; **Wolchok, Jedd D.**

CORPORATE SOURCE: Donaldson-Atwood Cancer Clinic and Flaherty Comparative Oncology Laboratory, The E&M Bobst Hospital of the Animal Medical Center, New York, NY, 10021, USA

SOURCE: Clinical Cancer Research (2003), 9(4), 1284-1290
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Canine malignant **melanoma** (CMM) is a spontaneous, aggressive, and metastatic neoplasm. Preclin. mouse studies have shown that

xenogeneic DNA vaccination with genes encoding tyrosinase family members can induce antibody and cytotoxic T-cell responses, resulting in tumor rejection. These studies provided the rationale for a trial of **xenogeneic** DNA vaccination in CMM using the human tyrosinase gene. Three cohorts of three dogs each with advanced (WHO stage II, III, or IV) CMM received four biweekly i.m. injections (dose levels 100, 500, or 1500 μg, resp./vaccination) of human tyrosinase plasmid DNA i.m. via the Biojector2000 delivery device. Mild local reactions at injection sites were the only toxicities observed, with no signs of autoimmunity. One dog with stage IV disease had a complete clin. response in multiple lung metastases for 329 days. Two dogs with stage IV disease had long-term survivals (421 and 588+ days) in the face of significant bulky metastatic disease, and two other dogs with locally controlled stage II/III disease had long-term survivals (501 and 496 days) with no evidence of **melanoma** on necropsy. Four other dogs were euthanized because of progression of the primary tumor. The Kaplan-Meier median survival time for all nine dogs was 389 days. The results of this trial demonstrate that **xenogeneic** DNA vaccination of dogs with advanced malignant **melanoma** is a safe and potentially therapeutic modality. On the basis of these results, addnl. evaluation of this novel therapeutic is warranted in locally controlled CMM and advanced human **melanoma.**

CC 1-6 (Pharmacology)
Section cross-reference(s): 15

ST dog malignant **melanoma** antitumor DNA vaccination
xenogeneic tyrosinase gene

IT Vaccines
(DNA; long-term survival of dogs with advanced malignant **melanoma** after DNA vaccination with **xenogeneic** human tyrosinase)

IT Canis familiaris
Drug targets
Human
Immunotherapy
Melanoma
(long-term survival of dogs with advanced malignant **melanoma** after DNA vaccination with **xenogeneic** human tyrosinase)

IT Antitumor agents
(malignant **melanoma**; long-term survival of dogs with advanced malignant **melanoma** after DNA vaccination with **xenogeneic** human tyrosinase)

IT DNA
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaccine; long-term survival of dogs with advanced malignant **melanoma** after DNA vaccination with **xenogeneic** human tyrosinase)

IT 9002-10-2, Tyrosinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tyrosinase, DNA encoding, drug target; long-term survival of dogs with advanced malignant **melanoma** after DNA vaccination with **xenogeneic** human tyrosinase)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:794136 HCAPLUS
DOCUMENT NUMBER: 137:309482
TITLE: Compositions for treatment of **melanoma** and method of using same

INVENTOR(S): **Houghton, Alan N.; Bergman, Philip J.; Wolchok, Jedd D.**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U. S. Ser. No. 627,694.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002150589	A1	20021017	US 2001-996128	20011127
WO 9825574	A2	19980618	WO 1997-US22669	19971210
WO 9825574	A3	19980903		
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6328969	B1	20011211	US 1999-308697	19990521
PRIORITY APPLN. INFO.:			US 1996-32535P P	19961210
			US 1997-36419P P	19970217
			WO 1997-US22669 W	19971210
			US 1999-308697 A2	19990521
			US 2000-180651P P	20000126
			US 2000-627694 A2	20000728

AB **Melanoma** can be treated in a mammalian subject by administering to the subject an immunol.-effective amount of a **xenogeneic melanoma**-associated differentiation antigen. For example, genetic immunization with a plasmid containing a sequence encoding human gp75 has been shown to be effective in treatment of dogs with **melanoma.**

IC ICM A61K039-00
ICS C12N009-64
NCL 424185100
CC 15-2 (Immunochemistry)
Section cross-reference(s): 63
ST **melanoma** vaccine antigen gp75 tyrosinase sequence
IT Animal cell line
(B16 **melanoma**; vaccine compns. for treatment of **melanoma** and method of using same)
IT Glycoproteins
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(gp75; vaccine compns. for treatment of **melanoma** and method of using same)
IT Cell differentiation
(inducers; vaccine compns. for treatment of **melanoma** and method of using same)
IT Antigens
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(tumor-associated; vaccine compns. for treatment of **melanoma** and method of using same)
IT Vaccines
(tumor; vaccine compns. for treatment of **melanoma** and method of using same)
IT Antitumor agents
Canis familiaris
Gene therapy

Genetic vectors
Human
Immunization
Melanoma
Mus
Plasmid vectors
Plasmids
(vaccine compns. for treatment of **melanoma** and method of using same)

IT Promoter (genetic element)
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(vaccine compns. for treatment of **melanoma** and method of using same)

IT Antitumor agents
(vaccines; vaccine compns. for treatment of **melanoma** and method of using same)

IT 473006-17-6, DNA (plasmid htyr-pING+) 473006-18-7, DNA (plasmid mtyr-pING+)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; vaccine compns. for treatment of **melanoma** and method of using same)

IT 9002-10-2, Tyrosinase
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(vaccine compns. for treatment of **melanoma** and method of using same)

L8 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:43903 HCAPLUS
DOCUMENT NUMBER: 137:92289
TITLE: **Xenogeneic** DNA Immunization in **Melanoma** Models for Minimal Residual Disease
AUTHOR(S): Hawkins, William G.; Gold, Jason S.; Blachere, Nathalie E.; Bowne, Wilbur B.; Hoos, Axel; Lewis, Jonathan J.; **Houghton, Alan N.**
CORPORATE SOURCE: Swim Across America Laboratory, Departments of Surgery & Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Journal of Surgical Research (2002), 102(2), 137-143
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Introduction. DNA immunization with **xenogeneic** genes encoding homologous antigens protects mice against tumor challenge with syngeneic **melanoma** in a lung metastasis model. The effect of **xenogeneic** human TRP-2 (hTRP2) DNA immunization on disease confined to an orthotopic site, the skin, and in a model of minimal residual disease that is relevant to a setting of adjuvant therapy for micrometastatic cancer is reported. Methods. Immunization and tumor challenge with B16F10LM3 **melanoma** were performed in C57BL/6 mice and in mice genetically deficient in MHC class I or II mols. A **melanoma** variant of B16 with a predilection for lung metastasis was selected and used to challenge C57BL/6 mice. Tumor challenge in the footpad with the B16 variant was followed by local tumor growth and lung metastasis. The tumor-bearing distal extremities were surgically resected

and mice were randomized to receive hTRP2 DNA immunization or no treatment. Approx. 3-5 wk after surgical resection, lungs were harvested and metastases counted. Results. **Xenogeneic** DNA immunization with hTRP2 prevented tumor growth in the skin by a mechanism requiring CD4+ and CD8+ T cells but did not inhibit the growth of established tumors. Adjuvant immunization with hTRP2 DNA after resection significantly reduced lung metastases and decreased local recurrence rates after surgical resection. Conclusions. **Xenogeneic** DNA immunization with hTRP2 was effective in protecting mice from intradermal tumor challenge. Immunization prevented local recurrence and the development of metastases in a mouse model of minimal residual disease, supporting a role for DNA immunization against melanosomal antigens as an adjuvant to surgery in high-risk primary **melanomas.** (c) 2002 Academic Press.

CC 15-2 (Immunochemistry)

ST trp2 gene T lymphocyte vaccine **melanoma**

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MHC (major histocompatibility complex), class I; **xenogeneic** DNA immunization in **melanoma** models for minimal residual disease)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MHC (major histocompatibility complex), class II; **xenogeneic** DNA immunization in **melanoma** models for minimal residual disease)

IT Proteins
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRP-2 (tyrosinase-related protein 2); **xenogeneic** DNA immunization in **melanoma** models for minimal residual disease)

IT Immunostimulants
(adjuvants; **xenogeneic** DNA immunization in **melanoma** models for minimal residual disease)

IT Lung, neoplasm
(metastasis, from **melanoma**; **xenogeneic** DNA immunization in **melanoma** models for minimal residual disease)

IT Vaccines
(tumor; **xenogeneic** DNA immunization in **melanoma** models for minimal residual disease)

IT Antitumor agents
(vaccines; **xenogeneic** DNA immunization in **melanoma** models for minimal residual disease)

IT CD4-positive T cell
CD8-positive T cell
Disease models
Human
Immunotherapy
Melanoma
Surgery
(**xenogeneic** DNA immunization in **melanoma** models for minimal residual disease)

IT DNA
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**xenogeneic** DNA immunization in **melanoma** models for minimal residual disease)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:119790 HCAPLUS
DOCUMENT NUMBER: 135:120901
TITLE: **Xenogeneic** DNA vaccination prevents metastasis in a **melanoma** model of minimal residual disease
AUTHOR(S): Hawkins, William G.; Gold, Jason S.; **Houghton, Alan N.**; Lewis, Jonathan J.
CORPORATE SOURCE: Departments of Surgery and Immunology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
SOURCE: Surgical Forum (2000), 51, 265-266
CODEN: SUFOAX; ISSN: 0071-8041
PUBLISHER: American College of Surgeons
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Xenogeneic** DNA immunization with human TRP-2 (hTRP2) is capable of protecting mice against challenge with syngeneic **melanoma.** Immunol. therapy has not been as successful in the treatment of established tumors. One explanation is that the tumor induces tolerance and may prevent development of a cytotoxic T-cell response. An orthotopic model of mouse **melanoma** in which tumor burden is minimal, and spontaneous metastases occur in a predictable manner, has been developed. Immune response in this model may be more relevant to the clin. setting in which the primary tumor has been resected and the patient remains at high risk for the development of metastases. A study was conducted to determine whether DNA vaccination could prevent metastases in this model of minimal residual disease. The findings showed that **xenogeneic** DNA immunization with TRP-2 was effective in preventing the development of metastases in a mouse model of minimal residual disease. These results support a role for immunotherapeutic strategies as an adjuvant to surgery by demonstrating that an effective antitumor response is possible in the presence of micrometastases. In addition, this model provides a method for the preclin. assessment of antimetastatic tumor immunity.

CC 15-2 (Immunochemistry)
ST DNA vaccine **melanoma** metastasis isomerase immunotherapy
IT Immunostimulants
(adjuvants; **xenogeneic** DNA vaccination prevents metastasis in a **melanoma** model of minimal residual disease)
IT Neoplasm
(metastasis; **xenogeneic** DNA vaccination prevents metastasis in a **melanoma** model of minimal residual disease)
IT Immunotherapy
Melanoma
(**xenogeneic** DNA vaccination prevents metastasis in a **melanoma** model of minimal residual disease)
IT DNA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**xenogeneic** DNA vaccination prevents metastasis in a **melanoma** model of minimal residual disease)
IT 130122-81-5, Dopachrome Δ-isomerase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**xenogeneic** DNA vaccination prevents metastasis in a **melanoma** model of minimal residual disease)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:799448 HCAPLUS
DOCUMENT NUMBER: 132:92212
TITLE: Coupling and uncoupling of tumor immunity and autoimmunity
AUTHOR(S): Bowne, Wilbur B.; Srinivasan, Roopa; **Wolchok, Jedd D.**; Hawkins, William G.; Blachere, Nathalie E.; Dyall, Ruben; Lewis, Jonathan J.; **Houghton, Alan N.**
CORPORATE SOURCE: Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Journal of Experimental Medicine (1999), 190(11), 1717-1722
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Self-antigens, in the form of differentiation antigens, are commonly recognized by the immune system on **melanoma** and other cancers. We have shown previously that active immunization of mice against the melanocyte differentiation antigen, a tyrosinase-related protein (TRP) gp75TRP-1 (the brown locus protein) expressed by **melanomas**, could induce tumor immunity and autoimmunity manifested as depigmentation. In this system, tumor immunity and autoimmunity were mediated by autoantibodies. Here, we characterize immunity against another tyrosinase family glycoprotein TRP-2 (the slaty locus protein), using the same mouse model and method of immunization. As observed previously for gp75TRP-1, immunity was induced by DNA immunization against a **xenogeneic** form of TRP-2, but not against the syngeneic gene, and depended on CD4+ cells. Immunization against TRP-2 induced autoantibodies and autoreactive cytotoxic T cells. In contrast to immunization against gp75TRP-1, both tumor immunity and autoimmunity required CD8+ T cells, but not antibodies. Only autoimmunity required perforin, whereas tumor immunity proceeded in the absence of perforin. Thus, immunity induced against two closely related autoantigens that are highly conserved throughout vertebrate evolution involved qual. different mechanisms, i.e., antibody vs. CD8+ T cell. However, both pathways led to tumor immunity and identical phenotypic manifestations of autoimmunity.

CC 15-8 (Immunochemistry)
ST tumor immunity autoimmunity TRP2 gene immunization
IT Glycoproteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(TRP-2; tumor immunity and autoimmunity by DNA immunization with TRP-2 glycoprotein)
IT Antibodies
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(autoantibodies; tumor immunity and autoimmunity by DNA immunization with TRP-2 glycoprotein)
IT Immunity
(autoimmunity; tumor immunity and autoimmunity by DNA immunization with TRP-2 glycoprotein)
IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(slaty; tumor immunity and autoimmunity by DNA immunization with TRP-2 glycoprotein in relation to)
IT Neoplasm

(tumor immunity and autoimmunity by DNA immunization with TRP-2 glycoprotein)
IT CD8-positive T cell
(tumor immunity and autoimmunity by DNA immunization with TRP-2 glycoprotein in relation to)
IT Perforin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor immunity and autoimmunity by DNA immunization with TRP-2 glycoprotein in relation to)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:747477 HCAPLUS
DOCUMENT NUMBER: 126:30063
TITLE: Immune response to a differentiation antigen induced by altered antigen: a study of tumor rejection and autoimmunity
AUTHOR(S): Naftzger, Clarissa; Takechi, Yoshizumi; Kohda, Hironobu; Hara, Isao; Vijayasaradhi, Setaluri; **Houghton, Alan N.**
CORPORATE SOURCE: Swim Across America Lab., Memorial Sloan-Kettering Cancer Cent., New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1996), 93(25), 14809-14814
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recognition of self is emerging as a theme for the immune recognition of human cancer. One question is whether the immune system can actively respond to normal tissue autoantigens expressed by cancer cells. A second but related question is whether immune recognition of tissue autoantigens can actually induce tumor rejection. To address these issues, a mouse model was developed to investigate immune responses to a melanocyte differentiation antigen, tyrosinase-related protein 1 (or gp75), which is the product of the brown locus. In mice, immunization with purified syngeneic gp75 or syngeneic cells expressing gp75 failed to elicit antibody or cytotoxic T-cell responses to gp75, even when different immune adjuvants and cytokines were included. However, immunization with altered sources of gp75 antigen, in the form of either syngeneic gp75 expressed in insect cells or human gp75, elicited autoantibodies to gp75. Immunized mice rejected metastatic **melanomas** and developed patchy depigmentation in their coats. These studies support a model of tolerance maintained to a melanocyte differentiation antigen where tolerance can be broken by presenting sources of altered antigen (e.g., homologous **xenogeneic** protein or protein expressed in insect cells). Immune responses induced with these sources of altered antigen reacted with various processed forms of native, syngeneic protein and could induce both tumor rejection and autoimmunity.
CC 15-2 (Immunochemistry)
ST differentiation antigen tumor rejection autoimmunity
IT Immunity
(autoimmunity; immune response to a differentiation antigen induced by altered antigen: a study of tumor rejection and autoimmunity)
IT Antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(differentiation; immune response to a differentiation antigen induced by altered antigen: a study of tumor rejection and autoimmunity)

IT Sialoglycoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gp75, tyrosinase-related protein 1; immune response to a differentiation antigen induced by altered antigen: a study of tumor rejection and autoimmunity)
IT Melanocyte
(immune response to a differentiation antigen induced by altered antigen: a study of tumor rejection and autoimmunity)
IT **Melanoma**
(metastasis; immune response to a differentiation antigen induced by altered antigen: a study of tumor rejection and autoimmunity)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT